

REMARKS

Introductory Comments:

Claims 1-22 were examined in the Office Action under reply and stand rejected under 35 U.S.C. §112, first paragraph. This rejection is respectfully traversed as discussed more fully below. Applicants note with appreciation the withdrawal of the previous rejections under 35 U.S.C. §112, second paragraph and 35 U.S.C. §102.

Overview of the Above Amendments:

Claims 1, 3, 4, 7 and 8 have been cancelled. Claims 2 and 5 have been amended to depend from claim 12 rather than cancelled claim 1. Claims 2, 5 and 6 have therefore been amended to track the language of claim 12 from which these claims now either directly or ultimately depend. Additionally, claims 2, 5, 6, 10, 12 and 13 have been amended to replace the recitation of 75% sequence identity with 90% sequence identity.

Support for these amendments can be found in the claims as originally filed, as well as throughout the specification at, e.g., page 14, line 23. Cancellation of claims 1, 3, 4, 7 and 8 and amendment of claims 2, 5, 6, 10, 12 and 13 is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications containing the unamended claims.

Rejection Under 35 U.S.C. §112, First Paragraph:

Claims 1-22 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Office disputes applicants' assertion that expression levels from a construct including a deleted Intron A sequence as claimed could achieve greater expression than levels from a corresponding construct completely lacking the Intron A sequence:

[A]pplicants have not demonstrated that any of the fragments direct the transcription of a coding sequence to levels greater than those levels achieved by a corresponding construct that completely lacks an Intron A sequence. While applicants argue that it would be presumed by the skilled artisan that fragments that direct expression of a coding sequence to levels greater than the full intron, there is no evidence to indicate this is true. In fact, given that a deletion in the Intron A fragment leads to levels of expression that are greater than a full length fragment, a skilled artisan could also conclude that a construct with further deletions would lead to even greater levels of transactivation such that the levels of expression from a construct without Intron A would be greater than those of the instant invention.

Office Action, pages 5-6, bridging paragraph. However, applicants respectfully disagree.

In particular, it is well known that constructs including the Intron A sequence provide greatly enhanced expression levels over constructs lacking this regulatory region. See, e.g., Chapman et al., *Nucleic Acids Res.* (1991) 19:3979-3986. Thus, it is contrary to the conventional wisdom that levels of expression from a construct without the Intron A sequence would provide greater expression levels than those achieved with a construct as claimed. In fact, there would be every expectation that at least equal levels would be achieved using constructs as claimed. Nevertheless, in an effort to advance prosecution, all claims now either ultimately or directly depend from claim 12 which recites that the expression construct provides for levels of expression equal to, or greater than, those levels achieved by an expression construct that includes a corresponding intact, full-length Intron A sequence. Applicants have provided evidence that a number of Intron A sequences with varying deletions indeed provide expression levels equal to, or greater than a parent vector containing the full-length Intron A sequence. See, Example 2 and Figure 4 of the application. Accordingly, the Examiner's concern with regard to the comparison with a construct completely lacking an Intron A sequence has been obviated.

The Office also asserts:

[T]he specification lacks disclosure as to the relevant identifying characteristics of Intron A fragments lacking at least 10 internal nucleotides and comprising nucleotides having at least 75% sequence identity to nucleotides at positions 1-25 and 775-820 that would be able to direct expression of a coding sequence to levels greater than that of a vector without Intron A.

* * *

In an unpredictable art, the disclosure of one example in one genus would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of the claimed genus.

Office Action, page 6. However, applicants disagree.

As an initial matter, applicants note several of the claims subject to the present rejection do not include the recitation of 75% sequence identity. Specifically, this limitation is absent from claims 9, 11, 15, 16, 18 and 20-22. Moreover, applicants submit for reasons of record that the relevant identifying characteristics of a fragment as recited are indeed detailed in the specification and that they have provided an adequate number of species to support the generic claims. As previously explained, applicants have described multiple species falling within the scope of the claims in the application as filed. Example 2 describes results of experiments done using 13 different constructs with varying Intron A deletions. All but two of the 13 constructs exhibited expression levels higher than achieved with the parent construct that retained the full-length Intron A sequence. See, Figure 4 of the application.

Not only have applicants described multiple species falling within the generic claims, applicants have provided a starting structure, i.e., the sequences described in Figures 1-3 and Table 1, and provided functional characteristics, namely, increased expression, coupled with known as well as a disclosed correlation between structure and function. Applicants have further taught that a variety of plasmids including various deletions of the Intron A sequence provide for enhanced expression levels. Finally, throughout the specification applicants teach the regions of the Intron A sequence contemplated for deletion or change. See, e.g., page 8, line 18 through page 9, line 14, pages 9-10, bridging paragraph; page 17, line 6 through page 18, line 13; pages 19-10, bridging paragraph.

Applicants remind the Examiner there is no fixed number of species that must be disclosed to satisfy the written description requirement:

A “representative number of species” means that the species that are adequately described are representative of the entire genus. ... What constitutes a “representative number” is an inverse function of the skill and knowledge of the art. Satisfactory disclosure of a “representative number” depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. ... Description of a representative number of species does not require the description be of such specificity that it would provide individual support for each species that the genus embraces.

Final Examiner Guidelines on Written Description, 66 Fed. Reg. 1099, emphasis added. Indeed, the Patent Office's “Synopsis of Application of Written Description Guidelines” is clear that a single disclosed species may be representative of a “product-by-function” genus when all members exhibit structural identity to a reference compound and when an assay is provided for identifying all variants having the claimed activity. Example 14 of the Synopsis is reproduced below:

Claim:

A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of $A \rightarrow B$.

Analysis:

... The procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art.

There is actual reduction to practice of a single disclosed species. The specification indicates that the genus of proteins that must be variants of SEQ ID NO:3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO:3. The **single species disclosed** is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity. One of skill in the art would conclude

that applicant was in possession of the necessary common attributes possessed by the members of the genus.

Conclusion: The disclosure meets the requirements of 35 U.S.C. § 112, first paragraph as providing adequate written description for the claimed invention. (Example 14, emphasis added.)

Like Example 14, applicants in the pending case have provided a limit to the structural identity (now 90% identity), a specified activity of the variants (directs the transcription of a coding sequence present in the construct at levels equal to, or greater than, those levels achieved by an expression construct that includes a corresponding intact, full-length Intron A sequence) and methods for identifying constructs exhibiting the specified activity (See, e.g., Example 2 of the application). Therefore, as in PTO Example 14, the multiple species disclosed in the application are representative of the genus as a whole.

Accordingly, one of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus, and it is clear that, as concluded in PTO Example 14, the written description of these claims in the pending case provides adequate written description for the claimed invention. Withdrawal of the rejection under 35 U.S.C. §121, first paragraph is therefore respectfully requested.

CONCLUSION


Applicants respectfully submit that the claims define a patentable invention.
Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Please direct all further written communications in this application to:

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Respectfully submitted,

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